PATENT COOPERATION TREAT

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
DU-PWO-024		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2007/012685	30/05/2007	30/05/2006
Applicant		
DUKE UNIVERSITY		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [ ] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 2a
      [X] as suggested by the applicant
      [ ] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

ernational application No
PCT/US2007/012685

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBASE, BIOSIS, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PITTMAN J ET AL: "INTEGRATED MODELING OF CLINICAL AND GENE EXPRESSION INFORMATION FOR PERSONALIZED PREDICTION OF DISEASE OUTCOMES" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 101, no. 22, 1 June 2004 (2004-06-01), pages 8431-8436, XP007900270 ISSN: 0027-8424	72,73, 83-93
Y	the whole document page 8431, right-hand column	1-58,72, 73,94

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[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 February 2008	03/03/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Leber, Thomas

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Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NEVINS J R ET AL: "Towards integrated clinico-genomic models for personalized medicine: Combining gene expression signatures and clinical factors in breast cancer outcomes prediction" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 12, no. Review Issue 1, 15 October 2003 (2003-10-15), pages R153-R157, XP009096400 ISSN: 0964-6906	72,73, 83-91
Y		1-73
X	HUANG E ET AL: "Gene expression predictors of breast cancer outcomes" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 361, no. 9369, 10 May 2003 (2003-05-10), pages 1590-1596, XP004424192 ISSN: 0140-6736	72,73, 83-93
Y	the whole document page 1591, left-hand column	1-73,94
X	THACH D C ET AL: "Surveillance of transcriptomes in basic military trainees with normal, febrile respiratory illness, and convalescent phenotypes." GENES AND IMMUNITY OCT 2005, vol. 6, no. 7, October 2005 (2005-10), pages 588-595, XP009096417 ISSN: 1466-4879 abstract	92,93
X	KASAMATSU A ET AL: "Identification of candidate genes associated with salivary adenoid cystic carcinomas using combined comparative genomic hybridization and oligonucleotide microarray analyses" INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY, EXETER, GB, vol. 37, no. 9, September 2005 (2005-09), pages 1869-1880, XP004974399 ISSN: 1357-2725 abstract	92,93

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HARPOLE DAVID H JR ET AL: "A prognostic model of recurrence and death in stage I non-small cell lung cancer utilizing presentation, histopathology, and oncoprotein expression" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 55, no. 1, 1 January 1995 (1995-01-01), pages 51-56, XP009093546 ISSN: 0008-5472 abstract	72,73
Y	KWIATKOWSKI D J ET AL: "Molecular pathologic substaging in 244 stage I non-small-cell lung cancer patients: Clinical implications" JOURNAL OF CLINICAL ONCOLOGY, GRUNE AND STRATTON, NEW YORK, NY, US, vol. 16, no. 7, 1998, pages 2468-2477, XP009096353 ISSN: 0732-183X abstract	72,73
A	WALL M E ET AL: "SINGULAR VALUE DECOMPOSITION AND PRINCIPAL COMPONENT ANALYSIS" A PRACTICAL APPROACH TO MICROARRAY DATA ANALYSIS, BOSTON, MA : KLUWER ACADEMIC PUBL, US, 2003, pages 91-109, XP007900285 ISBN: 1-4020-7260-0 the whole document	
A	HUANG E ET AL: "GENE EXPRESSION PROFILING FOR PREDICTION OF CLINICAL CHARACTERISTICS OF BREAST CANCER" RECENT PROGRESS IN HORMONE RESEARCH, ACADEMIC PRESS, NEW YORK, NY, US, vol. 58, 2003, pages 55-73, XP008043332 ISSN: 0079-9963 the whole document	
P,X	POTTI ANIL ET AL: "A genomic strategy to refine prognosis in early-stage non-small-cell lung cancer" NEW ENGLAND JOURNAL OF MEDICINE, MASSACHUSETTS MEDICAL SOCIETY, BOSTON, MA, US, vol. 355, no. 6, 10 August 2006 (2006-08-10), pages 570-580, XP009096340 ISSN: 1533-4406 the whole document	1-94

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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2007/012685	30.05.2007	30.05.2006

International Patent Classification (IPC) or both national classification and IPC
INV. C12Q1/68

Applicant
DUKE UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

Due: 6-3-08

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

DOCKETED

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Date of completion of this opinion
see form PCT/ISA/210
Date: 4-29-08 CG

Authorized Officer
Leber, Thomas

Also on docket

Telephone No. +49 89 2399-7195

Form (PCT/ISA/237) (Cover Sheet) (April 2005)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

see separate sheet

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-71,74-82,94

because:

☒ the said international application, or the said claims Nos. 1-57,74-82(IA) relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 94 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 1-71(partly)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-71,74-82,94
	No:	Claims	72,73,83-93
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-94
Industrial applicability (IA)	Yes:	Claims	58-73,83-94
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II
Priority

1. The priority of the present application appears to be valid (Art 8, Rule 4.10 PCT).

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 15, which is dependent on claim 1, comprises the feature of "providing adjuvant chemotherapy to a subject...". Similarly, claim 74 comprises the feature of "obtaining an NSCLC sample from a subject". Claims 1 and 74 thus comprise subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of claim 1, 74 and dependent claims 2-57 and 75-82 (Article 34(4)(a)(i) PCT).

2. Claim 1 refers to a method for determining the likelihood of developing "tumor recurrence". The method steps, however, aim to predict the likelihood of "developing tumor metastasis", which represents a particular form of tumor recurrence. Claim 1 thus lacks clarity (Art 6 PCT). Moreover, having regard to the description and the examples, in particular, it is noted that none of groups of samples analysed (Duke, ACOSOG Z0030 and CALGB 9761) provide information to tumor recurrence by metastasis, but only to tumour recurrence in general (page 53, line 31 - page 54, line 26). Claim 1 thus lacks support by the description (Art 6 PCT) and the application enablement (Art 5 PCT) to the extent as this claim refers to the prediction of the likelihood to develop tumor metastasis. Search and consequently also examination of claim 1 and claims 2-57 was thus limited to the prediction of the likelihood tumor recurrence.
   For the same reasons, search and examination also for claims 58-71 was limited to the identification of clusters associated with tumor recurrence.

3. Claim 94 refers to a kit comprising a gene chip of claims "120-121". It is noted that

the present application does not comprise any claims 120 or 121. It is assumed that these reference numbers represent a clerical error and should actually refer to the gene chip defined in claims 92 or 93 just preceding claim 94. The international search and examination was thus carried out on this basis.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Basis for the assessment of novelty, inventive step and industrial applicability

1.1 Reference is made to the following document/s/:

D1: PITTMAN J ET AL: "INTEGRATED MODELING OF CLINICAL AND GENE EXPRESSION INFORMATION FOR PERSONALIZED PREDICTION OF DISEASE OUTCOMES" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 101, no. 22, 1 June 2004 (2004-06-01), pages 8431-8436, XP007900270 ISSN: 0027-8424

D2: NEVINS J R ET AL: "Towards integrated clinico-genomic models for personalized medicine: Combining gene expression signatures and clinical factors in breast cancer outcomes prediction" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 12, no. Review Issue 1, 15 October 2003 (2003-10-15), pages R153-R157, XP009096400 ISSN: 0964-6906

D3: HUANG E ET AL: "Gene expression predictors of breast cancer outcomes" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 361, no. 9369, 10 May 2003 (2003-05-10), pages 1590-1596, XP004424192 ISSN: 0140-6736

D4: THACH D C ET AL: "Surveillance of transcriptomes in basic military trainees with normal, febrile respiratory illness, and convalescent phenotypes." GENES AND IMMUNITY OCT 2005, vol. 6, no. 7, October 2005 (2005-10), pages 588-595, XP009096417 ISSN: 1466-4879

D5: KASAMATSU A ET AL: "Identification of candidate genes associated with

salivary adenoid cystic carcinomas using combined comparative genomic hybridization and oligonucleotide microarray analyses" INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY, EXETER, GB, vol. 37, no. 9, September 2005 (2005-09), pages 1869-1880, XP004974399 ISSN: 1357-2725

D6: HARPOLE DAVID H JR ET AL: "A prognostic model of recurrence and death in stage I non-small cell lung cancer utilizing presentation, histopathology, and oncoprotein expression" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 55, no. 1, 1 January 1995 (1995-01-01), pages 51-56, XP009093546 ISSN: 0008-5472

D7: KWIATKOWSKI D J ET AL: "Molecular pathologic substaging in 244 stage I non-small-cell lung cancer patients: Clinical implications" JOURNAL OF CLINICAL ONCOLOGY, GRUNE AND STRATTON, NEW YORK, NY, US, vol. 16, no. 7, 1998, pages 2468-2477, XP009096353 ISSN: 0732-183X

2. Novelty

2.1 Claims 1-71 appear to be novel over the available prior art (Art 33(2) PCT).

2.2 Document D1 discloses a method for modelling gene expression data in order to predict breast cancer recurrence. The method is based on comparing gene expression data from tumour samples of subjects showing different patterns of tumour recurrence, determination of metagenes, single value decomposition analysis and averaging the predictions on the basis of various statistical tree models, each node including a statistical predictive probability of tumour recurrence (D1, whole document).

Although not explicitly stated, it is immediately clear that the analysis performed in D1 was carried out using a computer readable medium. The subject-matter of claim 72 is thus implicitly disclosed in D1. Moreover, D1 discloses thereby also the binary prediction tree modelling as specified in claim 73 and also the computer readable medium as specified in claim 83. Claims 72, 73 and 83-91 lack thus novelty over D1 (Art 33(2) PCT).

The same subject-matter is also disclosed in D2 and D3 (D2, D3: whole document).

Claims 72, 73 and 83-91 thus lack also novelty over D2 and D3 (Art 33(2) PCT).

2.3 The oligonucleotide arrays U133 plus 2.0 and U133A as used in the present application (page 54, line 19; page 55, line 16) fall within the scope of present claim 92 and 93. As shown by documents D4 and D5, both arrays represent prior art (D5, abstract; D4, abstract). Thus, claims 92 and 93 lacks novelty over D4 and D5 (Art 33(2) PCT). Moreover, these genes are also present on the Affymetrix U95Av2 GeneChip used in D1 (D1, page 8431, right col.) and D3 (D3, page 1591, left col.). Thus, claims 92 and 93 lack novelty over D1 and D3 (Art 33(2) PCT).

3. Inventive step

3.1 Claim 94 differs from the disclosure of D1 and D3 only by providing the array and the analysis software in form of a kit.
The technical effect resulting from this difference appears to reside in the provision of the reagents necessary to carry out a particular method in a useful form.
The technical problem appears to be the provision of the assay reagents in a useful form.
It appears that an inventive step (Art 33(3) PCT) can not be acknowledged for the solution provided in claim 94 as it is a standard procedure for the skilled person to convert a successful laboratory method in to a kit which permits the less experienced to perform a technically demanding technique. Thus, claim 94 lacks an inventive step (Art 33(3) PCT).

3.2 As detailed in item 2.2 above, documents D1-D3 disclose the analytical method of gene expression data as specified in claims 72 and 73 and which are part of present claim 1 (features ii) and iii)).
The subject-matter of present claim 1 thus differs from the disclosure of any of D1 only in that tumour recurrence of non-small cell lung cancer (NSCLC) is determined whereas in D1, breast cancer is analysed.
It would appear that this difference fails to generate any technical effect that has not already been achieved in D1. In fact, both D1 and the present application achieve the same technical effect, namely the definition of metagenes the expression of which

can be analysed to predict the likelihood for tumor recurrence.
Starting from D1, the skilled person is confronted with the technical problem of providing an alternative tumor type to carry out the same study.
The skilled person confronted with this technical problem would consult the prior art to find an alternative tumor for the analysis. The selection of NSCLC thereby appears to represent an arbitrary selection among the many tumor the skilled person could use. Documents D6 and D7, for example, disclose attempts to predict recurrence for NSCLC on the basis of clinical presentation and the expression of a limited number of marker genes (D6 and D7, abstract).
A similar line of reasoning could also be put forward on the basis of documents D2 and D3. Thus, claim 1 lacks also an inventive step in view of D2 and D3 (Art 33(3) PCT).

3.3 Independent claim 58 refers to a method for defining a statistical tree model predictive of NSCLC tumor recurrence. Similar to claim 1, this claim also comprises the analytical steps already disclosed in any of D1-D3. This claim thus differs from closest prior art document D1 thus by the same difference from D1 and claim 1, namely the selection of the NSCLC tumor and for the same reasons as detailed above, also claim 58 lacks an inventive step (Art 33(3) PCT). Consequently, claim 58 also lacks an inventive step over D2 and D3 for the same reasons as claim 1 (Art 33(3) PCT).

3.4 Dependent claims 2-57 and 59-71 appear not to contain any features which in combination with the claims to which they refer could possibly meet the requirements for inventive step under Art 33(3) PCT as the features of the said dependent claims merely cover embodiments that fall into the range of the conventional for the skilled person and as none of the said features appears to be associated with a technical effect that would go beyond the effect the skilled person would immediately associate with it. Thus, also the said dependent claims fail to comply with Art 33(3) PCT for inventive step.

4. Industrial applicability

4.1 The subject-matter disclosed in the claims 58-73, 83-94 of the present application appears to be industrially applicable (Art 33(4) PCT).

4.2 For the assessment of the present claims 1-57 and 74-82 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII
Certain defects in the international application

1. The expression "herein incorporated by reference" or equivalents thereof (e.g. page 1, line 6, page 11, lines 10-11, page 49, line 27 or page 63, lines 21-22) does not comply with the Guidelines, Section IV, II-4.17.

2. The reference to unpublished documents (e.g. page 1, lines 4-5) does not comply with the Guidelines, Section IV, II-4.18.

3. The present application does not meet the requirements of Art 5 and Rule 5 PCT as documents D1-D7, which represent relevant prior art, are not referred to therein.

Re Item VIII
Certain observations on the international application

1. The term "multiple genes" in claim 1 seems to mean "at least two". The examples in the description, however, appears to suggest that thousands of genes need to be assessed for the method of claim 1. Thus claim 1 lacks support by the description over its full scope (Art 6 PCT). The same objection applies to claim 58 (Art 6 PCT).

2. Claim 83 refers to a computer readable medium which is defined by the data present on it. The Authority in charge of international examination is of the view that the said data as such fail to represent a technical feature according to Rule 6.3(a) PCT and thus cannot limit the scope of claim 83 (Art 6 PCT). The same applies to dependent claims 84-90 (Art 6 PCT).

3. Claim 16 defines the likelihood of tumor recurrence to be greater than "50%". This value, however, appears not to be a technical feature of the method as such but seems to define only the result to be achieved without, however, providing any definition of the technical features required to actually achieve this level of certainty. Claim 16 thus lacks clarity (Art 6 PCT). The same objection applies to claims 17, 18, 20-25, 53-57 and 63 (Art 6 PCT).